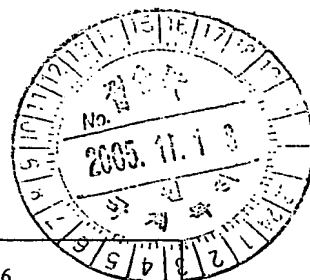


PATENT COOPERATION TREATY

PCT


INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference 4FPO-11-05	FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/KR2004/003426	International filing date(day/month/year) 23 DECEMBER 2004 (23.12.2004)	Priority date (day/month/year) 31 DECEMBER 2003 (31.12.2003)	
International Patent Classification (IPC) or national classification and IPC IPC7 A61K 31/56, A61P 35/00, A23L 1/29			
Applicant KOREA RESEARCH INSTITUTE OF BIOSCIENCE AND BIOTECHNOLOGY et al			

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____ containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>	
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input checked="" type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>	

Date of submission of the demand 27 JULY 2005 (27.07.2005)	Date of completion of this report 14 NOVEMBER 2005 (14.11.2005)
Name and mailing address of the IPEA/KR  Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Authorized officer LEE, Mi Jeong Telephone No. 82-42-481-5601

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[Signature]

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

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Box No. 1 Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This report is based on translations from the original language into the following language _____ which is the language of a translation furnished for the purposes of:
 - ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
 - ☒ the international application as originally filed/furnished

 - ☐ the description:
 - pages _____ as originally filed/furnished
 - pages* _____ received by this Authority on _____
 - pages* _____ received by this Authority on _____

 - ☐ the claims:
 - pages _____ as originally filed/furnished
 - pages* _____ as amended (together with any statement) under Article 19
 - pages* _____ received by this Authority on _____
 - pages* _____ received by this Authority on _____

 - ☐ the drawings:
 - pages _____ as originally filed/furnished
 - pages* _____ received by this Authority on _____
 - pages* _____ received by this Authority on _____

 - ☐ the sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:
 - ☐ the description, pages _____
 - ☐ the claims, Nos. _____
 - ☐ the drawings, sheets _____
 - ☐ the sequence listing (*specify*): _____
 - ☐ any table(s) related to sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
 - ☐ the description, pages _____
 - ☐ the claims, Nos. _____
 - ☐ the drawings, sheets _____
 - ☐ the sequence listing (*specify*): _____
 - ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

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Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees the applicant has, within the applicable time limit:
 - ☐ restricted the claims
 - ☐ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☐ neither restricted nor paid additional fees.
2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is :
 - ☐ complied with.
 - ☒ not complied with for the following reasons:

Group I. Claims 1-5 relate to a pharmaceutical composition for preventing and treating cancer comprising a Cinnamoni Cortex extract including a compound of formula 1 and a Zizyphi Fructus extract including a compound of formula 2.

Group II. Claim 6 relates to functional food for preventing and treating cancer comprising the said active ingredients.

Although both Group I and II are relevant to the composition comprising the same active ingredients, there is no technical relationship between a pharmaceutical composition and functional food.
4. Consequently, this report has been established in respect of the following parts of the international application :
 - ☒ all parts.
 - ☐ the parts relating to claims Nos.

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. Statement**

Novelty (N)	Claims	1 - 6	YES
	Claims		NO
Inventive step (IS)	Claims	1 - 6	YES
	Claims		NO
Industrial applicability (IA)	Claims	1 - 6	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The following documents are referred to in this report:

- D1: Planta Med. Vol.65(3), pp.263-266 (1999 Apr.)
D2: Biochem. Pharmacol. Vol.65(8), pp.1343-1350 (2003 Apr.)
D3: Cancer Res. Vol.48(4), pp.938-942 (1988 Feb.)
D4: Head Neck. Vol.25(9), pp.732-740 (2003 Sep)
D5: J. Invest. Dermatol. Vol.114(5), pp.935-940 (2000 May)

1. Novelty and Inventive Step

Claims 1-5 of the present invention relate to a pharmaceutical composition for preventing and treating cancer comprising a Cinnamoni Cortex extract including a compound of formula 1(2'-hydroxycinnamaldehyde) and a Zizyphi Fructus extract including a compound of formula 2(betulinic acid). Claim 6 of the present invention relates to functional food for preventing and treating cancer comprising the said active ingredients.

D1 discloses that 2'-hydroxycinnamaldehyde strongly inhibits in vitro growth of 29 kinds of human cancer cells and in vivo growth of SW-620 human tumor xenograft without the loss of body weight in nude mice.

D2 discloses that CB403 is synthesized from 2'-hydroxycinnamaldehyde and CB403 inhibits tumor growth in a concentration-dependent manner.

D3 discloses synergistic cell inactivation of human NHIK 3025 cells by cinnamaldehyde in combination with cis-diamminedichloroplatinum(II).

D4 discloses that betulinic acid is a new cytotoxic compound against malignant head and neck cancer cells.

D5 discloses that betulinic acid suppresses the growth and colony-forming ability of all human melanoma cell lines investigated and the effect of betulinic acid on growth inhibition in combination with ionizing radiation was additive in colony-forming assays.

Each of 2'-hydroxycinnamaldehyde and betulinic acid is disclosed to have anticancer activity when used alone in D1-D5. However, none of D1-D5 discloses a composition comprising the two active ingredients mentioned in claims 1-6 of the present invention.

(Continued on the Supplemental Sheet.)

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:

Box V.

Furthermore, there is no implication or suggestion to lead those who skilled in the art to expect that the combination of the said active ingredients has a synergistic effect in inhibiting the growth of cancer cells in D1-D5.

Therefore, the novelty and inventive step of the claims 1-6 in the present invention can be acknowledged over D1-D5 [Article 33(2) and 33(3) PCT].

2. Industrial Applicability

The subject-matter of claims 1-6 appears to be industrially applicable [Article 33(4) PCT].